

REMARKS

Claims 1-11 and 14-17 are pending for prosecution.
Claims 1 and 14 have been amended to more distinctly describe the invention. No new subject matter is believed to have been added.

In the Office Action dated February 12, 2008, the Examiner rejected under 35 U.S.C. §102 claims 1-3 as anticipated by Gray et al. (U.S. 6,399,571) and claims 12 and 13 as anticipated by Idusogie et al. (U.S. 6,242,195). Applicants responded to this rejection on August 12, 2008 explaining how the claims differed from the prior art. Applicants assume that the Examiner agreed with the arguments presented by the Applicants as this rejection has not been repeated.

Similarly, in the Office Action dated February 12, 2008, the Examiner rejected the claims under 35 U.S.C. §103 as unpatentable over:

- (i) Tuse et al. in view of Hashimoto et al.
(claims 1, 4, 5, 9, 11 and 12);
- (ii) Tuse et al. in view of Hashimoto et al. and Gray et al.
(claims 2 and 3);
- (iii) Tuse et al. in view of Hashimoto et al. in view of Gray et al. (claims 6-8),
- (iv) Tuse et al. and Hashimoto in view of Harman et al.
(claim 10);
- (v) Tuse et al. and Hashimoto in view of Foster et al.
(claims 13 and 17).

Applicants responded to this rejection on August 12, 2008 explaining how the claims differed from the prior art. Applicants assume that the Examiner agreed with the arguments presented by the Applicants as this rejection has not been repeated.

New Rejection under 35 U.S.C §103

In the Office Action dated December 10, 2008, the Examiner rejected the claims as unpatentable over:

- (i) Hashimoto et al. in view of Chong et al. and Novokhatny et al. (claims 1, 9 and 11);
- (ii) Hashimoto et al. in view of Chong et al., Novokhatny et al. and Gray et al. (claims 2, 3, 6-8)
- (iii) Hashimoto et al. in view of Chong et al., Novokhatny et al. and Tuse et al. (Claims 4, 5)
- (iv) Hashimoto et al. in view of Chong et al., Novokhatny et al. and Harman et al. (Claim 10)
- (v) Hashimoto et al. in view of Chong et al., Novokhatny et al., Gray et al., Tuse et al. and Foster et al. (Claims 14-17).

Claim 1 in the present application states:

A method for specifically detecting chitin and not cellulose in a sample containing chitin and cellulose, comprising the steps of:

- (a) contacting the sample with a first reagent comprising a chitin-binding domain (CBD) which is fused to a maltose-binding domain (MBD); and
- (b) detecting specifically whether chitin and not cellulose is present in the sample by the binding of the CBD in the CBD-MBD fusion to chitin.

The references cited against the claims are discussed individually and in various combinations below. Because of the large number of references that the Examiner combined in making the rejection, a table is also presented which summarizes the teaching of each reference at the end of the discussion. This table highlights the fact that no combination of references based on their teachings would describe the claimed invention. For example, no reference utilizes an MBP-CBD fusion protein as a reagent. Yet the use of MBP provides a means of detecting the binding of CBD to chitin in the claimed invention by immobilization of MBP to a substrate or attaching a reporter to MBP. (See also for example, Application page 13, line 27 to page 14, line 2 and examples.)

It should be noted that 5 of the 7 references were published after the filing and publication of patents on MBP and on CBD-intein-MBP fusion proteins (CBD-inteins: 5,496,714 (3/5/96), and 5,834,247 (11/10/98) and MBP: 5,643,758 (7/1/97)). Foster et al. and Tuse et al. were published earlier.

Since none of the later-filed cited references describe the use of MBP-CBD for the detection of chitin in a sample containing chitin and

cellulose, it can be deduced that despite the existence of individual components (MBP alone, CBD alone, and CBD fused to an intein and then to MBP), the novel use of reagents including MBP-CBD described in the present claimed invention was demonstrably not obvious to a person of ordinary skill in the art either at the time of the cited prior art or at the time the present application was filed.

Hashimoto et al.

There is no suggestion or teaching in this reference of a method for detection of chitin in a sample also containing cellulose even though Hashimoto et al. observe that CBD does not react with cellulose. In addition, there is no suggestion that a chitin-binding domain (CBD) fused to a maltose-binding domain (MBD) should be used in such detection.

The Examiner states that :

Hashimoto et al. differs from the instant invention in failing to teach the chitin binding domain is fused to a maltose binding protein. (p. 4 of office action)

However, Applicants assert that the Hashimoto et al. reference additionally fails to teach a detection method for chitin in the presence of cellulose or the need for such a detection method.

Chong et al.

This reference does not suggest, teach or provide motivation for a detection of the presence of chitin and not cellulose in a sample containing both chitin and cellulose which is the subject of the present claims.

This reference although referring to MBP fusion proteins does not correct the deficiencies in the Hashimoto et al. reference.

The Examiner states that:

Chong et al. teach that it is known in the art to construct fusion proteins comprising CBD fused to maltose binding protein. (p. 4 of the office action)

However, in the reference, MBP is not fused to CBD. Rather, MBP is fused to an intein which is fused to CBD (see Figure 1). The purpose of the Chong et al. reference is to purify protein using an intein system.

A person of ordinary skill in the art might refer to the Hashimoto et al. reference as a source of CBD for the described use of intein-mediated purification, but there is no teaching or motivation to construct the claimed method.

Novokhatny et al.

There is no suggestion or teaching in this reference of a method for detection of chitin in a sample also containing cellulose. In addition, there is no suggestion that a chitin-binding domain (CBD) fused to a maltose-binding domain (MBD) should be used in such detection.

Instead, this reference describes "the thermodynamics of [maltose binding protein] (MBP) unfolding ..." (p. 141)

as a carrier protein for the production of fusion proteins and for their purification, and determining "the value of differential scanning calorimetry for assessing the structural integrity of different fusion proteins." (p. 142)

However, the present claims are not directed to purification of a target protein. Instead, the present claims are directed to detection of a contaminant (chitin) in a sample also containing cellulose.

Gray et al.

The Examiner has added the Gray et al. reference to three other references in rejecting claims 2, 3 and 6-8 because of the use by Gray et al. of antibodies for detection.

However, the Hashimoto et al., Chong et al. and Novokhatney et al. references are not concerned with detection but rather describe methods of purification. The addition by the Examiner of the Gray et al. reference to the combination of references is the result of hindsight based on Applicants' claimed invention. A person of ordinary skill in the art would not be motivated to combine these four references based on the teachings in the references to achieve the claimed method. Even if the four references were combined, they would not teach the present claimed invention (see Table below).

Tuse et al.

This reference does not suggest, teach or provide motivation for a detection of the presence of chitin and not cellulose in a sample containing both chitin and cellulose which is the subject of the present claims using CBD-MBP.

Instead, Tuse et al. describe the use of chitinase and not the chitin-binding domain where the chitinous material is captured on a membrane and then the chitinase or chitinase fused to a reporter is exposed to the captured chitin to detect the chitin only.

In fact, Tuse et al. arguably contradict Hashimoto et al. because Tuse et al. utilize intact chitinase to "deduce the presence of chitin containing organisms in samples of all types of biological (mammalian and plant) tissues" (p. 5 lines 18-20). However, Hashimoto et al. state that "... chitinase AI exhibited weak but significant binding to cellulose in addition to various forms of insoluble chitin ..." (p. 3051). Hence, cross reactions would invalidate the approach described by Tuse et al.

Taking the five references as a whole, there is no basis except hindsight to believe that a person of ordinary skill in the art would be enabled to practice the claimed invention by the combination. Indeed, even if the five references were combined, they would not teach the claimed invention (see the Table below).

Foster et al.

This reference does not suggest, teach or provide motivation for a detection of the presence of chitin and not cellulose in a sample containing both chitin and cellulose which is the subject of the present claims.

Foster et al. describe an immunoassay with no reference to chitin, chitinase or chitin binding domains. This reference was filed 24 years before the present application was filed and appears to have little relevance to the claimed subject matter.

Harman et al.

This reference does not suggest, teach or provide motivation for a detection of the presence of chitin and not cellulose in a sample containing both chitin and cellulose which is the subject of the present claims.

Harman et al. do not describe or teach or suggest discrimination between cellulose and chitin. Nor does Harman et al. teach the use of MBP in a fusion protein. Nor does Harman et al. teach the use of a chitin-binding domain as compared with chitinase.

	Detect chitin not cellulose	MBP- CBD fusion	Sample with chitin and cellulose	MBP only	CBD only	Detect chitin with CBD	Detect chitin only with chitinase
Hashimoto (1999)	+	-	?	-	+	-	-
Chong (1997)	-	-	-	-	+	-	-
Novokhatney (1997)	-	-	-	+	-	-	-
Harman (2001)	-	-	-	-	-	-	+
Tuse (1991)	+	-	+	-	-	-	+
Grey (2002)	+	-	(+)	-	-	+	-
Foster (1984)	-	-	-	-	-	-	-
Claim 1 of app.	+	+	+	-	-	-	-

CONCLUSION

Applicants respectfully submit that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Applicants attach a petition for a three-month extension of time and authorize that \$555 be charged to Deposit Account No. 14-0740. Applicants authorize that any deficiencies be charged to the same Account.

Respectfully submitted,

NEW ENGLAND BIOLABS, INC.

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